

of an excess of phosgene, to effect the reaction of the amine hydrochloride, and to dehydrohalogenate the carbamoyl chloride. The reaction of amine hydrochlorides with phosgene is reported to be catalyzed by morpholine,³¹ boron trifluoride,³² aluminum chloride,³³ *N,N*-dialkylcarbamates,³⁴ *N,N*-dialkylamides,^{35,36} tetraalkylureas and thioureas,³⁵⁻³⁷ hexamethylphosphoramides,³⁵ or activated carbon.³⁸

Carbamoyl chlorides have been prepared by vapor-phase reaction of phosgene with primary amines.³⁹⁻⁴² Although this method is widely applicable, its greatest

utility lies in the preparation of the lower alkyl carbamoyl chlorides. Exposure of these alkyl carbamoyl chlorides to the conditions of the solvent phosgenation procedure leads to yield losses due to the formation of allophanoyl chlorides and isocyanate polymers. These carbamoyl chlorides are best converted to isocyanates by use of a tertiary amine acid acceptor, since conventional thermal dehydrohalogenation techniques lead to extensive degradation.

Isocyanates have also been prepared by the reaction of phosgene with primary amines in the presence of aqueous sodium hydroxide and an inert water insoluble solvent at low temperatures.⁴³

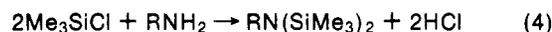
The kinetics of the reaction of phosgene with several aromatic amines has recently been examined,⁴⁴⁻⁴⁷ using a "quenching-flow" technique. The reactions follow second-order kinetics, and an SN₂ mechanism has been proposed.

Two methods are available by which primary amines can be "protected" prior to reaction with phosgene to minimize undesirable side reactions during the preparation of isocyanates.

The first method involves the reaction of primary amines with thionyl chloride to generate an *N*-sulfinyl derivative.⁴⁸ In the presence of a catalytic amount of pyridine or *N,N*-dimethylformamide, the sulfinyl derivative reacts with phosgene to afford the corresponding isocyanate and thionyl chloride.



In the second method,⁴⁹ the amine is treated with trimethylsilyl chloride and the derivatized amine is then treated with phosgene to give the isocyanate and regenerate the silylating agent.



When phosgene is treated with an excess of a primary or secondary amine, symmetrical ureas are produced in high yields. The reaction is usually carried out in the presence of an acid acceptor such as sodium hydroxide,⁵⁰ sodium carbonate,^{51,52} or pyridine.⁵³



Cyclic ureas can be prepared by the reaction of ethylenediamine or its derivatives with phosgene^{54,55} (eq 7).

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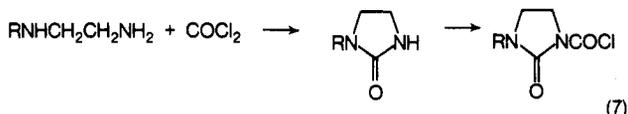
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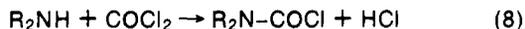
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In the case where R is the pentachlorophenyl group, phosgene reacts with the cyclic urea so readily that only the allophenyl chloride derivative could be isolated.⁵⁴



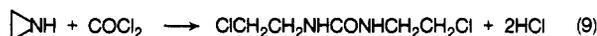
B. Reactions with Secondary Amines

Secondary amines react with phosgene to afford carbamoyl chlorides in excellent yields. The literature on this subject has recently been reviewed.⁵⁶



Although most *N,N*-dialkylcarbamoyl chlorides are fairly stable,⁵⁶ aziridinecarbamoyl chloride has never been isolated.^{57,58} Attempts to trap this elusive species as the triethylammonium or pyridinium salt have been unsuccessful.⁵⁸

When aziridine is added to an excess of phosgene, in the absence of an acid acceptor, bis(2-chloroethyl)urea is produced as the major product.^{58,59}

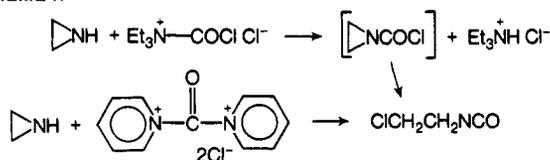


When equivalent amounts of aziridine and triethylamine in carbon tetrachloride are added to a solution containing 1 equiv of phosgene at -10°C , a mixture of bisaziridinyurea and 2-chloroethyl isocyanate is formed, the former being the major product.⁵⁸

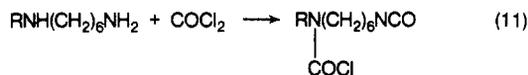


2-Chloroethyl isocyanate is the major product obtained when aziridine is allowed to react with an equivalent amount of 1:1 triethylamine-phosgene complex⁵⁷ or 2:1 pyridine-phosgene complex.⁵⁸ Aziridine carbamoyl chloride is postulated as a transient intermediate in this reaction (Scheme II).

SCHEME II



Compounds containing both an isocyanate and a carbamoyl chloride group have been prepared by reacting monoalkyl α,ω -diamines with phosgene.^{60,61}



One of the most useful methods for the preparation of oxazolidinones involves the reaction of phosgene with primary or secondary β -amino alcohols. This subject has been discussed in a recent review.⁶²

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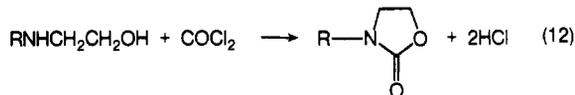
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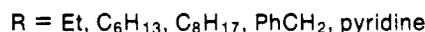
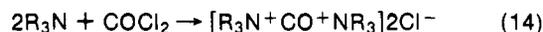
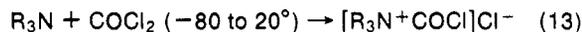
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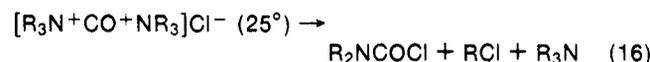
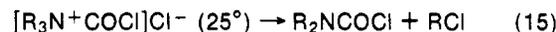
C. Reaction of Tertiary Amines

Phosgene reacts with alkyl tertiary amines at low temperatures to yield unstable crystalline complexes. In the case of lower alkyl tertiary amines, both 1:1 and 1:2 phosgene-amine complexes can be formed.^{58,63-66} The structures of these cationic complexes have been well established.^{48,58}



With higher alkyl tertiary amines (C_6 and greater), only the dicationic species could be obtained even in the presence of a large excess of phosgene.^{64,67}

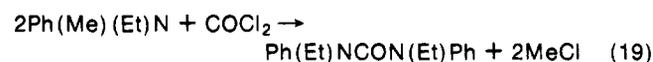
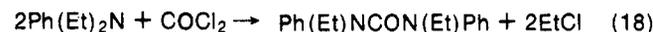
When tertiary amine-phosgene complexes are warmed to room temperature, they decompose to the corresponding *N,N*-dialkylcarbamoyl chlorides by eliminating a mole of alkyl chloride.^{63-66,68} The reaction of mixed alkyl tertiary amines with phosgene has not been studied.



When the reaction of excess phosgene with tertiary amines is carried out at elevated temperatures, secondary carbamoyl chlorides and alkyl halides are obtained directly in excellent yields.^{67,69} When the stoichiometry is reversed, and excess amine is used, excellent yields of tetrasubstituted ureas are obtained.^{63,70}



The use of mixed aryl-alkyl tertiary amines in the above reaction leads to the formation of symmetrical aryl-alkyl ureas.^{63,70}



Hexamethylenetetramine reacts with phosgene to afford a crystalline compound having the formula $(\text{C}_6\text{H}_{12}\text{N}_4)_2\text{COCl}_2$.⁷¹⁻⁷³ To our knowledge, the structure of this material has not been defined.

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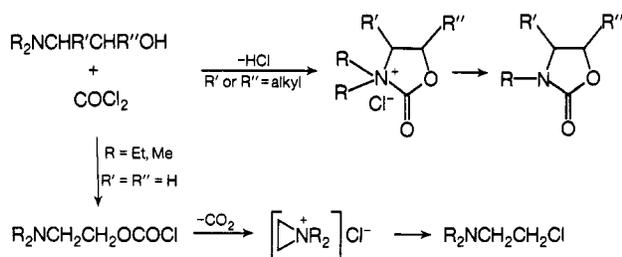
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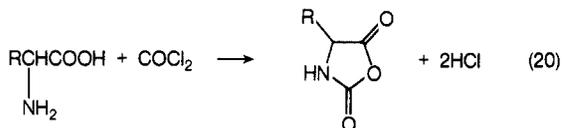
The reaction of phosgene with a series of 2-dialkylaminoalkanoic acids has recently been reported.⁷⁴ When either carbon of the aminoethanol bears an alkyl substituent, cyclization occurs to afford a 2-oxazolidinone derivative. Pyridine was used as an acid acceptor for the reaction and the heterocyclic products were obtained in good yield. When 2-diethylaminoethanol was subjected to the reaction conditions, the major product was shown to be 2-diethylaminoethyl chloride. Under carefully controlled conditions, 2-diethylaminoethyl chloroformate could be isolated and an aziridine intermediate was postulated to account for its facile decomposition. 2-Diethylaminoethyl chloroformate has also been prepared by reaction of 2-diethylaminoethanol hydrochloride with phosgene⁷⁵ (Scheme III).

SCHEME III



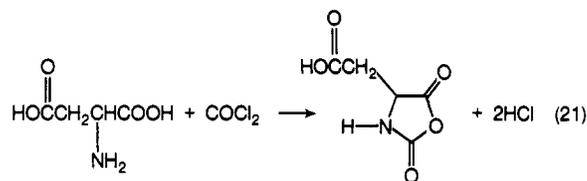
D. Reactions with Amino Acids

α -Amino acids react readily with phosgene, preferably in ether solvents, to afford oxazolidine-2,5-diones. These compounds are commonly called *N*-carboxy anhydrides or Leuchs' anhydrides. The synthetic method is sometimes referred to as the Fuchs-Farthing procedure and has been the topic of some recent reviews.⁷⁶⁻⁷⁹

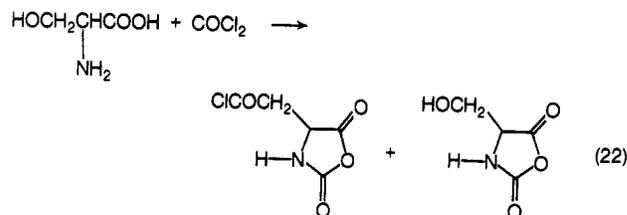


Some improvements in this preparation have been described⁸⁰⁻⁸¹ as well as the extension of this method to the synthesis of *N*-carboxy anhydrides (NCA's) of multifunctional amino acid derivatives which are useful in the synthesis of peptides.⁸²⁻⁸⁴

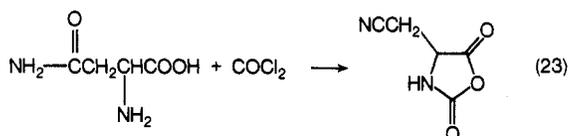
The presence of an additional carboxyl group in an amino acid does not alter the course of the reaction. Indeed, the phosgenation of aspartic acid apparently leads only to the formation of the α -NCA^{82,85} (eq 21).



If the amino acid contains a hydroxyl group (serine, threonine), chloroformate formation is a significant side reaction.⁸² The use of the silver salt of the amino acid as a starting material enables one to get a 50% yield of the desired NCA (eq 22).



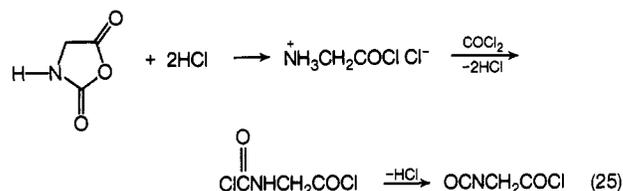
NCA's of amino acids bearing an amide group (asparagine, glutamine) cannot be prepared by the phosgenation procedure, since the amide group is readily dehydrated to a nitrile in the presence of phosgene^{82,86} (eq 23).



In some cases, when mild conditions are used, an intermediate *N*-chloroformyl derivative can be isolated from the reaction of an amino acid with phosgene.⁸⁶⁻⁹¹ Upon warming, these materials cyclize to afford the NCA (eq 24).



Under more strenuous conditions, and in the presence of hydrogen chloride, α -amino acids can be converted to 2-isocyanato acid chlorides.⁹²⁻⁹⁴ Reaction sequence 25 has been proposed to describe this transformation.



The facile degradation of NCA's by hydrogen chloride complicates their synthesis. The high yields of these products obtained in such solvents as tetrahydrofuran and dioxane can be attributed, in part, to the ability of these solvents to act as hydrogen chloride scavengers.

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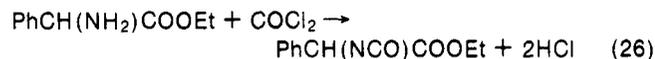
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Esters of α -amino acids react with phosgene in the expected fashion to give excellent yields of the corresponding isocyanates.⁹⁵⁻⁹⁷

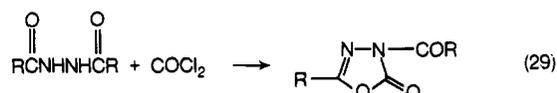
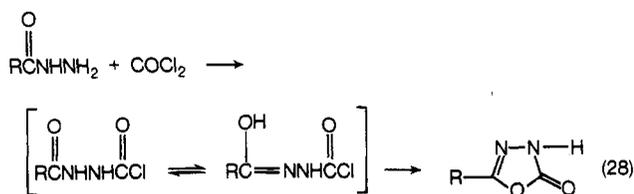


E. Reactions with Hydrazine Derivatives

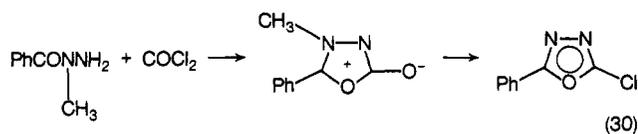
Hydrazine reacts with phosgene to afford good yields of carbonylhydrazide.^{98,99}



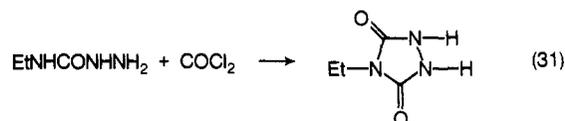
Acylated hydrazine derivatives yield 1,3,4-oxadiazole derivatives when treated with phosgene,^{98,100} providing a useful method of synthesizing this heterocyclic system (eq 28 and 29).



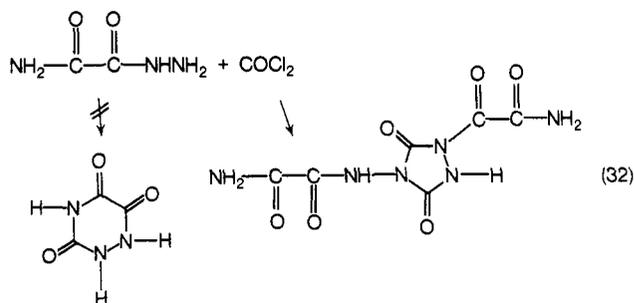
A similar reaction occurs when 1-benzoyl-1-methylhydrazine is treated with phosgene.¹⁰¹ The resulting sydnone will react further with phosgene to afford 2-chloro-5-phenyl-1,3,4-oxadiazole (eq 30).



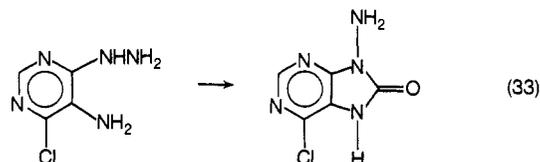
When semicarbazides are treated with phosgene, cyclization occurs to afford 1,2,4-triazole derivatives^{102,103} (eq 31).



An attempt to extend the above type of reaction to the synthesis of 1,2,4-triazine derivatives was unsuccessful.¹⁰⁴ The reaction of oxamic acid hydrazide with phosgene gave 4-oxamido-1-oxamoyl-1,2,4-triazolidine-3,5-dione as the only isolable reaction product (eq 32).



The reaction of phosgene with hydrazine derivatives has also been shown to be useful for the preparation of certain purine derivatives¹⁰⁵ (eq 33).

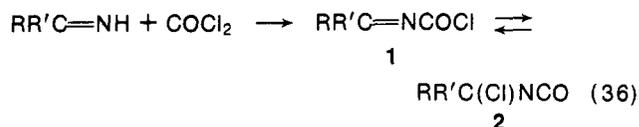
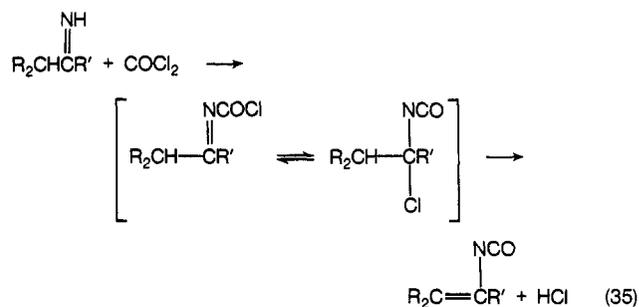


Dibenzophenonecarbohydrazone has been prepared by the reaction of benzophenone hydrazone with phosgene in the presence of pyridine.¹⁰⁶ An excess of phosgene must be avoided in this preparation, since the carbohydrazone derivative reacts further with phosgene to afford an unidentified product.



F. Reactions with Imino Compounds

The reaction of phosgene with ketimines having an α hydrogen leads to the formation of alkenyl isocyanates¹⁰⁷ (eq 35). When an α hydrogen is not available for elimination, an equilibrium mixture of products is formed.^{108,109} The relative amounts of the two products (1 and 2) depend on the nature of the substituents. For example, when $\text{R} = t\text{-Bu}$ and $\text{R}' = \text{Ph}$, only form 2 is observed, but when $\text{R} = \text{R}' = \text{Ph}$, approximately equal amounts of the two products are present as determined by an infrared study of the system.¹⁰⁹



(95) E. Kaiser, U. S. Patent 2,897,233 (1959); *Chem. Abstr.*, **54**, 328 (1960).

(96) J. D. Garber, R. A. Gasser, and D. Wasserman, French Patent 1,351,368 (1964); *Chem. Abstr.*, **60**, 15740 (1964).

(97) G. Losse and W. Goedicke, *Chem. Ber.*, **100**, 3314 (1967).

(98) T. Lieser and G. Nischk, *Chem. Ber.*, **82**, 527 (1949).

(99) O. Glemser, H. Weber, and H. Duyster, *Z. Anorg. Allg. Chem.*, **286**, 205 (1956); *Chem. Abstr.*, **51**, 4282 (1957).

(100) H. Reimlinger, J. Vandewalle, and W. Lingier, *Chem. Ber.*, **103**, 1934 (1970).

(101) C. Ainsworth, *Can. J. Chem.*, **43**, 1605 (1965).

(102) S. Kato, Japanese Patent 3122 (1956); *Chem. Abstr.*, **51**, 12983 (1957).

(103) H. Reimlinger, W. R. F. Lingier, J. M. Vandewalle, and E. Goes, *Synthesis*, **2**, 433 (1970).

(104) F. W. Ratz and H. Schroeder, *J. Org. Chem.*, **23**, 2017 (1958).

(105) M. H. Krackov and B. E. Christensen, *J. Org. Chem.*, **28**, 2677 (1963).

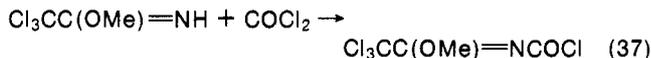
(106) P. W. West and J. Warkentin, *J. Org. Chem.*, **33**, 2089 (1968).

(107) L. I. Samarai, O. V. Vishevskii, and G. I. Derach, *Angew. Chem., Int. Ed. Engl.*, **6**, 21 (1967).

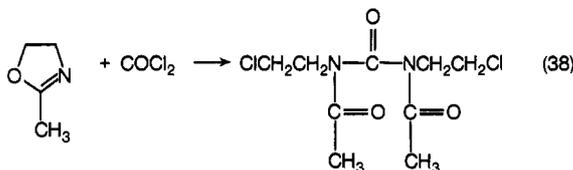
(108) (a) L. I. Samarai, V. P. Belaya, O. V. Vishevskii, and O. V. Derach, *Zh. Org. Khim.*, **7**, 20 (1968); (b) W. Seeliger, E. Aufderhaar, W. Diepers, R. Feinauer, R. Nehring, W. Thier, and H. Hellman, *Angew. Chem. Int. Ed. Engl.*, **5**, 875 (1966); (c) D. A. Tomalia, D. N. Ojha, and B. P. Thill, *J. Org. Chem.*, **34**, 1400 (1969).

(109) L. I. Samarai, O. V. Vishevskii, and O. V. Derach, *Chem. Ber.*, **102**, 2972 (1969).

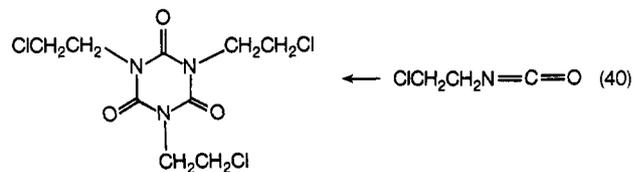
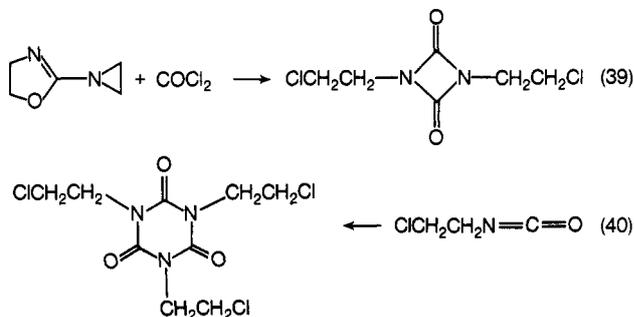
Imino esters react with phosgene to afford *N*-chloroformyl derivatives which are useful synthetic intermediates.^{108a}



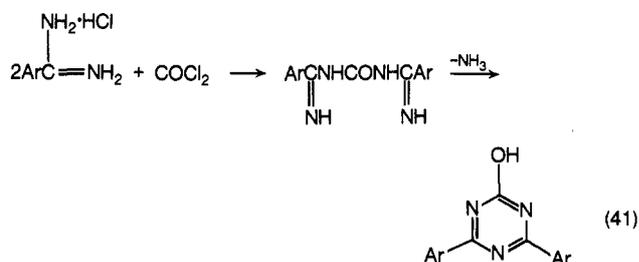
In contrast to the behavior of the acyclic imino esters, their cyclic analogs (2-oxazolines) undergo ring opening reactions with phosgene.^{108b,c} The reaction of 2-methyl-2-oxazoline with phosgene leads to the formation of 1,3-bis(2-chloroethyl)diacetylurea (eq 38), presumably by way of an oxazolinium salt.^{108b}



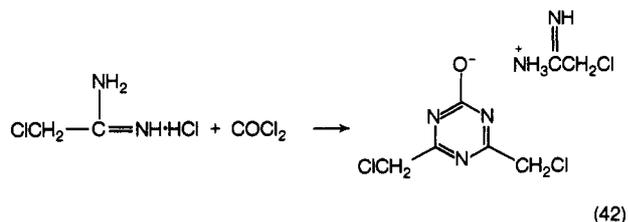
When 2-aziridinyl-2-oxazoline is treated with phosgene, the trimer of 2-chloroethyl isocyanate is obtained.^{108c} Chloroethyl isocyanate dimer is postulated as an intermediate in this reaction, formed by way of an oxazolinium salt (eq 39 and 40).



It has long been known¹¹⁰⁻¹¹³ that 2,4-diaryl-6-hydroxy-*s*-triazines can be prepared by the reaction of 1 mol of phosgene with 2 mol of an aryl amidine. The intermediate urea can, in most cases, be isolated if the reaction is run at low temperatures.^{112,113}



Attempts to extend the above reaction to the synthesis of alkyl triazine derivatives were unsuccessful.¹¹⁰ However, it has recently been shown¹¹⁴ that alkyl amidines



(110) A. Pinner, *Chem. Ber.*, **23**, 2919 (1890).

(111) T. Rappetort, *Chem. Ber.*, **34**, 1990 (1901).

(112) A. Pinner, *Chem. Ber.*, **28**, 473 (1895).

(113) C. Grundmann and H. Schroeder, *Chem. Ber.*, **87**, 747 (1954).

(114) H. Schroeder and C. Grundmann, *J. Amer. Chem. Soc.*, **78**, 2447 (1956).

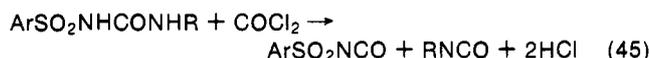
can be used in this reaction if the alkyl group bears an electron-withdrawing substituent (eq 42).

G. Reactions with Miscellaneous Nitrogen Compounds

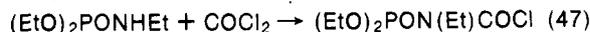
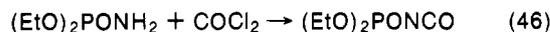
Aryl sulfonamides can be converted to sulfonyl isocyanates by reaction with phosgene.¹¹⁵⁻¹¹⁷ This reaction is sluggish and low yields are generally obtained.



It has recently been reported¹¹⁸ that reaction 43 can be catalyzed by alkyl isocyanates. This improvement stemmed from the discovery that arylsulfonyl ureas react readily with phosgene, under mild conditions, to afford arylsulfonyl isocyanates and alkyl isocyanates.



Phosphorus amides react with phosgene, in the presence of an acid acceptor, to give good yields of phosphorus isocyanates or carbamoyl chlorides.¹¹⁹

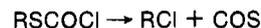
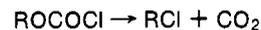
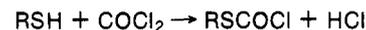


Phosgene reacts with *O*-substituted oxyamines to afford the corresponding oxycarbamoyl chloride derivatives.¹²⁰



III. Reactions at an Oxygen or Sulfur Center

Phosgene reacts with many different oxygen- or sulfur-bearing functional groups to produce a wide variety of useful and, in general, highly reactive products. Nearly all of the reactions discussed in this section involve, as the first step, the reaction of phosgene with an hydroxyl, thiol, or enolizable group to afford a chloroformyl derivative or intermediate. If the chloroformyl derivative is unstable, decomposition occurs to yield a chlorinated product.



A. Reactions with Alcohols and Thiols

The preparation of chloroformates by reaction of phosgene with alcohols or phenols has been discussed in detail in a recent review on chloroformate chemistry.⁶



(115) H. Krizikalla, German Patent 817.602 (1951); *Chem. Abstr.*, **47**, 2206 (1953).

(116) C. King, *J. Org. Chem.*, **25**, 352 (1960).

(117) F. Effenberger and R. Gleiter, *Chem. Ber.*, **97**, 1576 (1964).

(118) H. Ulrich, B. Tucker, and A. A. R. Sayigh, *J. Org. Chem.*, **31**, 2658 (1966).

(119) L. I. Samarai, O. I. Kolodyazhnyi, and G. I. Derach, *Zh. Obshch. Khim.*, **40**, 754 (1970); *Chem. Abstr.*, **73**, 24842 (1970).

(120) A. F. McKay, D. L. Garmaise, G. Y. Paris, and S. Gelblum, *Can. J. Chem.*, **38**, 343 (1960).

The reaction of phosgene with aliphatic hydroxy compounds is quite rapid¹⁰⁹ but reaction with phenols is slow, even at elevated temperatures. The use of acid acceptors (metal hydroxides, amines) to promote this reaction has been described.⁶ Recent work has shown that this reaction can be carried out in the absence of an acid acceptor when an *N,N*-dialkylamide¹²¹ or a quaternary ammonium salt¹²² is used as a catalyst.

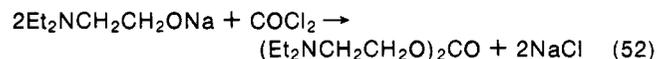
Alkyl and aryl thiols react with phosgene to afford chloroformyl derivatives. This reaction can be catalyzed by activated carbon,^{123,124} tertiary amines,^{125,126} or *N,N*-dialkylcarboxamides.¹²⁷



Symmetrical alkyl carbonates are common by-products formed during the preparation of alkyl chloroformates and result from the reaction of alcohols with the chloroformate.



The direct synthesis of alkyl carbonates can be carried out by adding phosgene to an excess of alcohol at elevated temperatures.⁶ Catalysis of this reaction by pyridine has been shown to be effective.^{128,129} The conversion of alcohols that bear other phosgene sensitive functional groups to carbonates has been accomplished by adding phosgene to the sodium alcoholate.¹³⁰

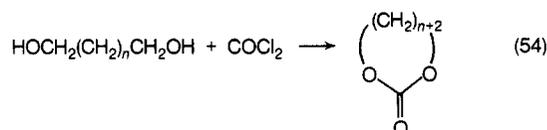


Symmetrical diaryl carbonates are prepared by adding phosgene to an excess of an alkali metal phenolate.¹³¹⁻¹³³ Similarly, *S,S'*-dialkyl dithiocarbonates can be prepared by adding phosgene to an excess of an alkali metal salt of a mercaptan.¹³⁴

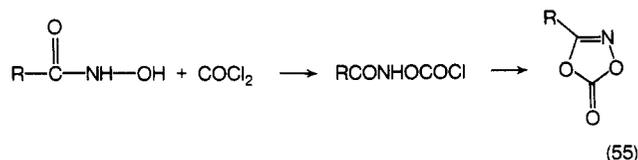


Cyclic carbonates are readily formed by the reaction of glycols with phosgene¹³⁵⁻¹³⁸ (eq 54). An acid acceptor is

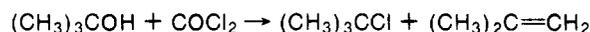
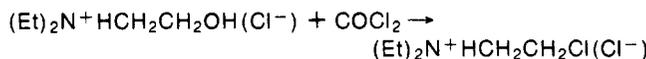
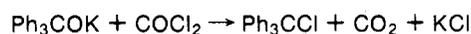
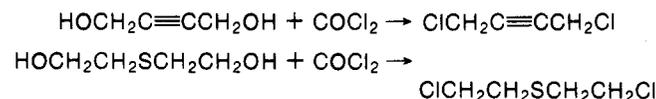
usually used to accelerate this transformation, and the carbonates of 1,2, 1,3, and 1,4 glycols have been prepared.¹³⁸



Hydroxamic acids have been reported to react with phosgene to yield chloroformyl derivatives,¹³⁹ and, under more strenuous conditions, nitrile carbonates.¹⁴⁰

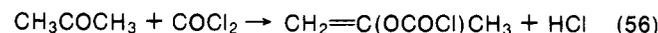


Activated alcohols can be converted to alkyl chlorides by reaction with phosgene in the presence of *N,N*-dimethylformamide.¹⁴¹ Because of the thermal instability of certain chloroformates, the production of halides can often occur in the absence of a catalyst.¹⁴²⁻¹⁴⁴ Most chloroformates are subject to facile decomposition in the presence of proper catalysts.⁶

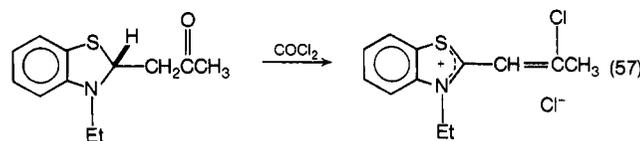


B. Reactions with Ketones

The preparation of isopropenyl chloroformate by the reaction of acetone with phosgene has been reported.¹⁴⁵



A similar reaction has been reported¹⁴⁶ to occur with the acetone derivative shown in eq 57. In this case, however, carbon dioxide is evolved and a chloropropene derivative is obtained.



The copper salt of 3,5,7-nonanetrione reacts with phosgene to afford a lactone,¹⁴⁷ presumably by way of an enol chloroformate.

(121) C. W. Stephens, U. S. Patent 3,211,744 (1966).

(122) R. J. Cotter, M. Matzner, and R. P. Kurkij, *Chem. Ind. (London)*, 791 (1965).

(123) Stauffer Chemical Co., British Patent 948,831 (1964); *Chem. Abstr.*, **60**, 11902 (1964).

(124) H. Tilles, U. S. Patent 3,093,537 (1963); *Chem. Abstr.*, **59**, 11271 (1963).

(125) H. Tilles, U. S. Patent 3,299,114 (1967); *Chem. Abstr.*, **66**, 75696 (1967).

(126) V. F. Mironov, V. P. Koxyukov, and V. D. Sheludyakov, *Zh. Obshch. Khim.*, **36**, 1860 (1966); *Chem. Abstr.*, **66**, 65577 (1967).

(127) H. Tilles, U. S. Patent 3,277,143 (1966); *Chem. Abstr.*, **66**, 2221 (1967).

(128) L. W. Kissinger, T. M. Benzinger, H. E. Ungnade, and R. K. Rowher, *J. Org. Chem.*, **28**, 2491 (1963).

(129) T. N. Hall, *J. Org. Chem.*, **33**, 4557 (1968).

(130) R. Reuber and H. Reinshagen, German Patent 887,650 (1953); *Chem. Abstr.*, **52**, 13807 (1958).

(131) Farbenfabriken Bayer A.-G., British Patent 841,654 (1960); *Chem. Abstr.*, **55**, 4433 (1961).

(132) J. M. Lee, U. S. Patent 2,837,555 (1958); *Chem. Abstr.*, **52**, 16214 (1958).

(133) R. S. Hanslick, W. F. Bruce, and A. Mascitti, *Org. Syn.*, **33**, 74 (1953).

(134) H. Pelster and H. Muehlbauer, German Patent 1,181,205 (1964); *Chem. Abstr.*, **62**, 6398 (1965).

(135) A. Contardi and A. Ercoli, *Gazz. Chim. Ital.*, **64**, 522 (1934); *Chem. Abstr.*, **29**, 1392 (1935).

(136) G. W. Moersch and A. C. Moore, U. S. Patent 2,587,641 (1952); *Chem. Abstr.*, **46**, 9601 (1952).

(137) B. J. Ludwig and E. C. Piech, *J. Amer. Chem. Soc.*, **73**, 5779 (1951).

(138) S. Sarel, L. A. Pohoryles, and R. Ben-Shoshan, *J. Org. Chem.*, **24**, 1873 (1959).

(139) M. Nakaishi and S. Inumura, Japanese Patent 70 02,376 (1970); *Chem. Abstr.*, **72**, 100321 (1970).

(140) Sinclair Research, Inc., Netherlands Patent 6,615,003 (1967); *Chem. Abstr.*, **67**, 81813 (1967).

(141) D. Ludsteck, G. Neubauer, H. Pasedach, and M. Seefelder, German Patent 1,133,716 (1962); *Chem. Abstr.*, **57**, 16396 (1962).

(142) P. Chao, *J. Chin. Chem. Soc. Taiwan*, **7**, 102 (1940); *Chem. Abstr.*, **35**, 5094 (1941).

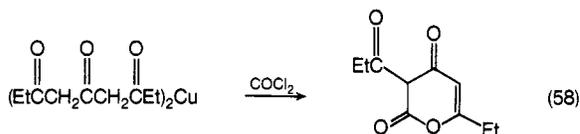
(143) S. T. Bowden and T. John, *J. Chem. Soc.*, 302 (1939).

(144) G. Cousserans and R. Amanrich, French Patent 1,383,121 (1964); *Chem. Abstr.*, **62**, 9009 (1965).

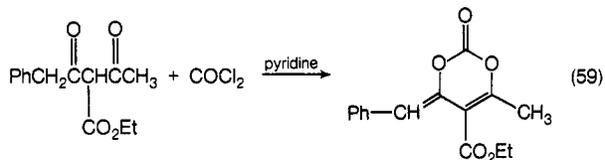
(145) M. P. Matusak, *J. Amer. Chem. Soc.*, **56**, 2007 (1934).

(146) N. N. Sveshnikov, I. I. Levkoev, N. I. Shirokova, and N. A. Damir, *Dokl. Akad. Nauk SSSR*, **148**, 1091 (1963); *Chem. Abstr.*, **59**, 6551 (1963).

(147) M. M. Mahala and S. S. Deshapande, *J. Indian Chem. Soc.*, **26**, 429 (1949).



Ethyl arylacetylacetoacetates react readily with phosgene, in the presence of pyridine, to produce cyclic carbonates.¹⁴⁸



C. Reactions of Carboxylic Acids and Derivatives

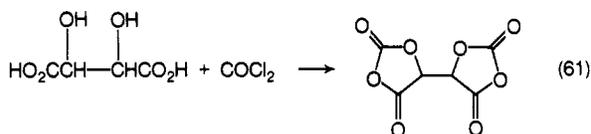
1. Carboxylic Acids

The use of phosgene for the conversion of carboxylic acids to acid chlorides has received much attention in recent years.



This reaction can be carried out at elevated temperature¹⁴⁹ or in the presence of catalysts such as *N,N*-dialkylcarboxamides,¹⁵⁰⁻¹⁵² tertiary amines,¹⁵³ thiocarboxamides,¹⁵⁰⁻¹⁵² or quaternary ammonium salts.¹⁵⁴ This procedure can also be used to convert sulfonic acids to sulfonyl chlorides.¹⁵⁵ The yields from the phosgenation procedure are comparable to those achieved by use of thionyl chloride or the phosphorus halides. The main advantage of this procedure is that the by-products are more easily disposed of than the waste products from alternate reagents, an item of considerable importance in this pollution conscious era.

Carboxylic acids that have an α -hydroxyl group react with phosgene to afford cyclic carbonates^{156,157} (eq 61). The carbonate formed from tartaric acid has been proposed as a carbonating agent for soft drinks because of its facile decomposition in water.¹⁵⁷



α -Mercaptocarboxylic acids are converted to the *S*-carboxy anhydride when treated with phosgene.¹⁵⁶

(148) K. H. Boltze and K. Heidenbluth, *Chem. Ber.*, **92**, 982 (1959).

(149) J. E. Carnahan, U. S. Patent 2,657,233 (1953); *Chem. Abstr.*, **48**, 12796 (1954).

(150) M. Seefelder, German Patent 1,167,819 (1964); *Chem. Abstr.*, **61**, 1761 (1964).

(151) C. F. Hauser, German Patent 1,931,074 (1970); *Chem. Abstr.*, **72**, 78472 (1970).

(152) H. Ulrich, B. Tucker, and A. A. R. Sayigh, *J. Org. Chem.*, **32**, 4052 (1967).

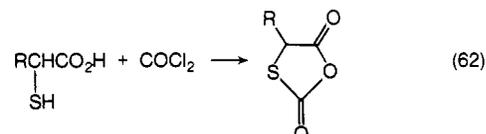
(153) Soc. pour l'ind. chim. à Bale, Swiss Patent 222,970 (1942); *Chem. Abstr.*, **43**, 2223 (1949).

(154) J. E. Carr, A. E. Kaye, and J. H. Wild, British Patent 1,159,266 (1969); *Chem. Abstr.*, **71**, 90862 (1969).

(155) H. H. Bosshard, R. Mory, M. Schmid, and H. Zollinger, *Helv. Chim. Acta*, **42**, 1653 (1959).

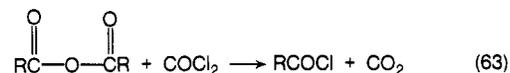
(156) W. H. Davies, British Patent 650,003 (1951); *Chem. Abstr.*, **45**, 8033 (1951).

(157) J. R. Feldman and R. L. Foltz, U. S. Patent 3,309,382 (1967).



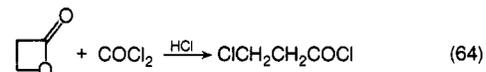
2. Carboxylic Acid Anhydrides

Carboxylic acid anhydrides react with phosgene in the presence of ferric chloride^{158,159} or *N,N*-dialkyl carboxamides¹⁶⁰ to produce acid chlorides. This method is more efficient than the direct conversion of acids to acid chlorides since both of the available chlorine atoms of phosgene are used in the reaction.



3. Lactones and Esters

When β -lactones are treated with phosgene, in the presence of HCl or aluminum chloride, ring opening occurs and β -chloro acid chlorides are produced.¹⁶¹ Pyridine has also been used as a catalyst for this reaction.^{162,163}

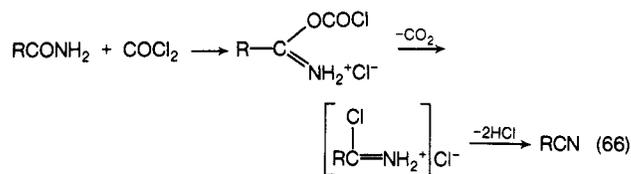


Alkyl esters of carboxylic acids are reported to undergo a similar reaction to afford an acid chloride and an alkyl halide.^{162,163} Esters are usually unreactive to normal phosgenation conditions and are often used as solvents in the synthesis of isocyanates, chloroformates, and other preparations.



4. Amides

Primary amides are readily dehydrated by phosgene to afford nitriles in excellent yields.¹⁶⁴⁻¹⁶⁷ Mechanism 66 has been suggested for this reaction.¹⁶⁶



When reaction 66 is carried out under pressure with excess phosgene, the reaction takes, to some extent, a different course to afford pyrimidine derivatives.¹⁶⁸ This is

(158) T. K. Brotherton, U. S. Patent 3,337,622 (1967); *Chem. Abstr.*, **67**, 90408 (1967).

(159) T. K. Brotherton, U. S. Patent 3,449,416 (1969).

(160) F. J. Chridtoph, Jr., S. H. Parker, and R. L. Seagraves, U. S. Patent 3,318,950 (1967); *Chem. Abstr.*, **67**, 43437 (1967).

(161) T. Nakabayashi, T. Matsumoto, and Y. Tanaka, *Kogyo Kagaku Zasshi*, **69**, 1245 (1966); *Chem. Abstr.*, **65**, 18700 (1966).

(162) K. Adam and H. Trieschmann, British Patent 743,557 (1956); *Chem. Abstr.*, **51**, 5819 (1957).

(163) K. Adam and H. Trieschmann, U. S. Patent 2,778,852 (1957); *Chem. Abstr.*, **51**, 8778 (1957).

(164) R. Greenhalgh, British Patent 488,036 (1938); *Chem. Abstr.*, **33**, 178 (1939).

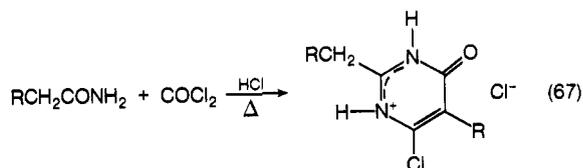
(165) M. J. Danzig, C. Y. Liang, and E. Passaglia, *J. Amer. Chem. Soc.*, **85**, 668 (1963).

(166) A. J. Speziale and L. P. Smith, *J. Org. Chem.*, **28**, 1805 (1963).

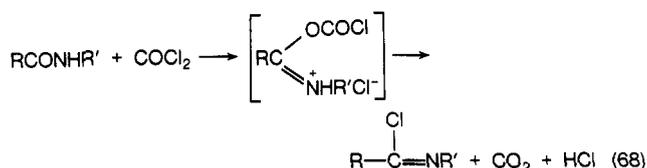
(167) W. Wilchek, S. Ariely, and A. Patchornik, *J. Org. Chem.*, **33**, 1258 (1968).

(168) S. Yanagida, H. Hayama, and S. Komori, *J. Org. Chem.*, **34**, 4180 (1969).

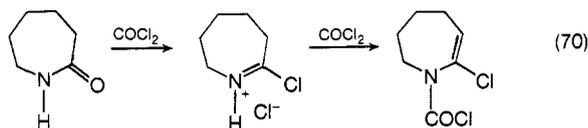
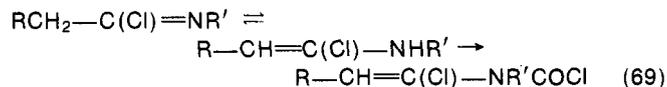
not surprising in view of the fact that phosgene has been shown to react with nitriles, in the presence of hydrogen chloride, to give the same type of product (see section IV.C).



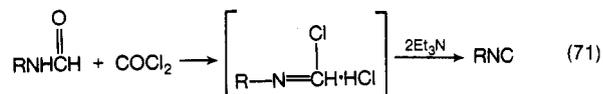
Monosubstituted amides react readily with phosgene to afford imidoyl chlorides¹⁶⁹⁻¹⁷¹ (eq 68). Although this transformation can be accomplished using other reagents (PCl_5 , POCl_3 , SOCl_2), phosgene is generally preferred due to the cleanliness of the reaction. Imidoyl halides are a very useful class of compounds and their preparation and reactions have been discussed in detail in a recent publication.¹⁷²



When the starting monosubstituted amide has a hydrogen available in the α position, the intermediate imidoyl chloride can react further with phosgene to yield an unsaturated carbamoyl chloride¹⁷³⁻¹⁷⁴ (eq 69 and 70).

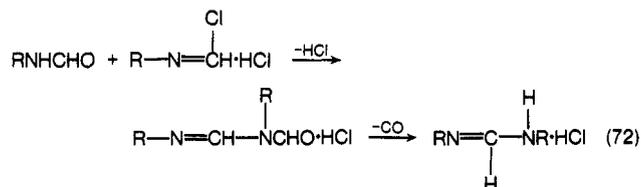


Phosgenation of *N*-substituted formamides affords an unstable imidoyl chloride which, in the presence of base, can be converted to an isocyanide in good yield.¹⁷⁵⁻¹⁷⁸

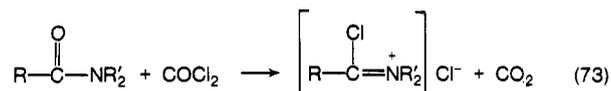


In the absence of base, the reaction takes a different course to afford formamidine salts as the major product.^{172,179-184} It has been proposed that formamidine

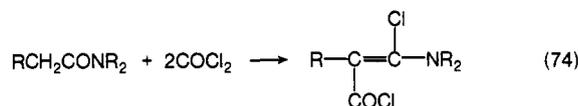
salt formation results from the reaction of the intermediate imidoyl chloride with unreacted amide.^{172,179,183}



N,N-Disubstituted carboxamides are halogenated by phosgene to give chloroiminium chlorides.¹⁸⁵⁻¹⁹⁴



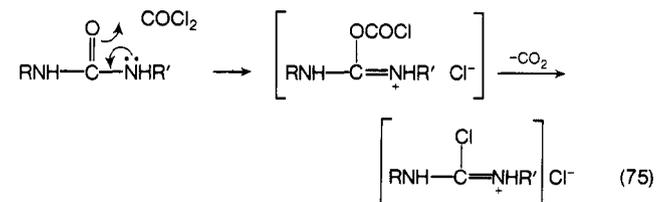
When the starting *N,N*-disubstituted amide has a hydrogen in the α position, further reaction can occur to yield an enamine derivative.¹⁹⁵



D. Reactions with Carbonic Acid Derivatives

1. Ureas and Thioureas

The reaction of phosgene with 1,3-disubstituted ureas follows two major pathways (eq 75 and 76). Attack at the urea oxygen leads to the formation of chloroformamidines,^{186,196-200} while attack at one of the urea nitrogen atoms affords allophanoyl chlorides.^{170,198,199}



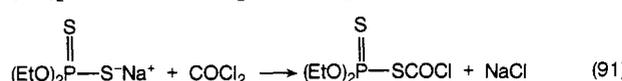
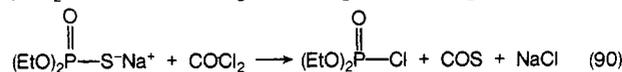
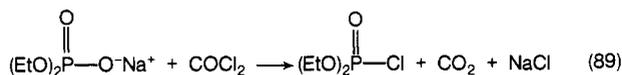
- (181) W. Jentzsch, *Chem. Ber.*, **97**, 2755 (1964).
 (182) W. Jentzsch and M. Seefelder, *Chem. Ber.*, **98**, 274 (1965).
 (183) A. A. R. Sayigh and H. Ulrich, *J. Chem. Soc.*, 3146 (1963).
 (184) W. H. Warren and F. E. Wilson, *Chem. Ber.*, **68**, 957 (1935).
 (185) H. Bredereck and K. Bredereck, *Chem. Ber.*, **94**, 2278 (1961).
 (186) H. Eillingsfeld, M. Seefelder, and H. Weidinger, *Angew. Chem.*, **72**, 836 (1960).
 (187) H. Eillingsfeld, M. Seefelder, and H. Weidinger, *Chem. Ber.*, **96**, 2671, 2899 (1963).
 (188) H. H. Bosshard, R. Mory, M. Schmid, and H. Zollinger, *Helv. Chim. Acta*, **42**, 1653 (1959).
 (189) Z. Arnold, *Chem. Listy*, **52**, 2013 (1958).
 (190) Z. Arnold, *Collect. Czech. Chem. Commun.*, **24**, 4048 (1959).
 (191) H. H. Bosshard and H. Zollinger, *Helv. Chim. Acta*, **42**, 1659 (1959).
 (192) W. Ziegenbein and W. Franke, *Chem. Ber.*, **93**, 1681 (1960).
 (193) Z. Arnold and J. Zemlicka, *Chem. Listy*, **52**, 458 (1952).
 (194) Z. Arnold and F. Sorn, *Chem. Listy*, **51**, 1082 (1957).
 (195) R. Buyle and H. G. Viehe, *Tetrahedron*, 4217 (1968).
 (196) H. Eillingsfeld, G. Neubauer, M. Seefelder, and H. Weidinger, *Chem. Ber.*, **97**, 1232 (1964).
 (197) H. Ulrich and A. A. R. Sayigh, *Angew. Chem., Int. Ed. Engl.*, **3**, 585 (1964).
 (198) H. Ulrich, J. N. Tilley, and A. A. R. Sayigh, *J. Org. Chem.*, **29**, 2401 (1964).
 (199) H. Ulrich and A. A. R. Sayigh, *Angew. Chem., Int. Ed. Engl.*, **5**, 704 (1966).
 (200) H. Ulrich and A. A. R. Sayigh, *J. Org. Chem.*, **30**, 2779 (1965).

- (169) V. Hahn and M. Grdinic, *J. Chem. Eng. Data*, **11**, 211 (1966).
 (170) I. Ugi, F. Beck, and U. Fetzer, *Chem. Ber.*, **95**, 126 (1962).
 (171) Stamicarbon N. V., Belgian Patent 609,822 (1962); *Chem. Abstr.*, **57**, 16505 (1962).
 (172) H. Ulrich, "The Chemistry of Imidoyl Halides," Plenum Press, New York, N. Y., 1968.
 (173) J. H. Ottenheim and J. W. Garritsen, German Patent 1,157,210 (1963); *Chem. Abstr.*, **60**, 6756 (1964).
 (174) J. H. Ottenheim and J. W. Garritsen, British Patent 901,169 (1962); *Chem. Abstr.*, **58**, 6810 (1963).
 (175) I. Ugi and R. Meyr, *Angew. Chem.*, **70**, 702 (1958).
 (176) I. Ugi and R. Meyr, *Chem. Ber.*, **93**, 239 (1960).
 (177) I. Ugi, W. Betz, U. Fetzer, and K. Offermann, *Chem. Ber.*, **94**, 2814 (1961).
 (178) Farbenfabriken Bayer A.-G., French Patent 2,002,568 (1969); *Chem. Abstr.*, **72**, 89824 (1970).
 (179) I. Hagedorn, H. Etling, and K. E. Lichtel, *Chem. Ber.*, **99**, 520 (1966).
 (180) W. Jentzsch, *Chem. Ber.*, **97**, 1361 (1964).

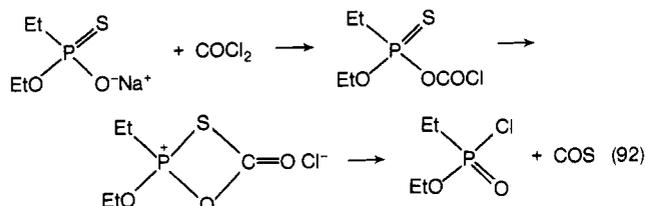
N,N-dialkyl dithiocarbamate salts are converted to thiuram monosulfides.²¹⁶

F. Reactions with Phosphorus Acid Derivatives

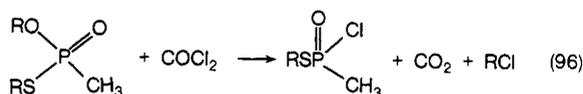
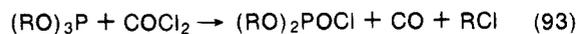
The salts of dialkyl phosphates or thiophosphates react with phosgene to give chloroformyl derivatives of varying stability.^{217,218} Decomposition of the chloroformyl derivative by elimination of carbon dioxide or carbon oxysulfide is often spontaneous and leads to the formation of phosphorus-halogen bonds.



The formation of a cyclic anhydride intermediate and subsequent decomposition has been postulated as a mechanism for the formation of chloridates. This concept is supported by the observation that optically active salts of ethyl ethylthiophosphonic acid react with phosgene to produce optically active ethyl ethylphosphonochloridate.²¹⁸



Phosgene reacts with a variety of phosphorus esters to yield alkyl chlorides and chlorinated phosphorus derivatives.²¹⁷⁻²²⁶ This type of reaction is known for both tri- and pentavalent phosphorus derivatives and is exemplified in the following equations.



(216) W. R. Trutna, U. S. Patent 3,133,966 (1964); *Chem. Abstr.*, **61**, 9408 (1964).

(217) J. Cadogan, *J. Chem. Soc.*, 3067 (1961).

(218) H. S. Aaron, R. T. Uyeda, H. F. Frack, and J. I. Miller, *J. Amer. Chem. Soc.*, **84**, 617 (1962).

(219) M. I. Kabachnik and P. A. Rossiskaya, *Bull. Acad. Sci. USSR*, **48**, (1957); *Chem. Abstr.*, **51**, 10366 (1957).

(220) M. Green and R. F. Hudson, *J. Chem. Soc.*, 1004 (1963).

(221) D. G. Doe, J. B. Perry, and R. K. Brown, *J. Chem. Soc.*, 3604 (1957).

(222) A. N. Pudovik and R. N. Platonova, *Zh. Obshch. Khim.*, **29**, 506 (1959); *Chem. Abstr.*, **54**, 254 (1960).

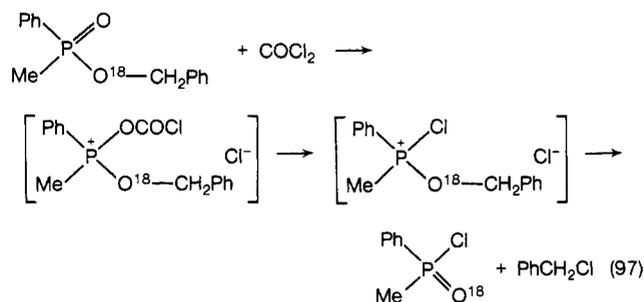
(223) K. A. Petrov, N. K. Bliznyuk, and V. E. Burygin, *Zh. Obshch. Khim.*, **29**, 1486 (1959); *Chem. Abstr.*, **54**, 8606 (1960).

(224) B. B. Brown, L. J. Lutz, C. A. Smith, Jr., and E. A. Weilmuenster, U. S. Patent 3,167,574 (1965); *Chem. Abstr.*, **62**, 10461 (1965).

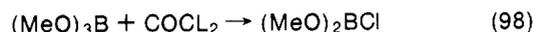
(225) M. Green and R. F. Hudson, *Proc. Chem. Soc., London*, 217 (1962).

(226) A. H. Ford-Moore, L. J. Lermitt, and C. Stratford, *J. Chem. Soc.*, 1777 (1953).

The mechanism of the reaction of pentavalent phosphorus derivatives with phosgene has recently been investigated using benzyl methylphenyl[O¹⁸]phosphinate as a model compound.²²⁰ Attack by phosgene occurs exclusively at the phosphoryl oxygen as illustrated in eq 97. Alternate mechanisms are discussed and dismissed as being inconsistent with the isotopic data.

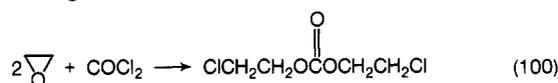
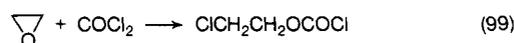


In a fashion similar to the phosphorus esters, trimethyl borate reacts with phosgene to give a chlorinated product.²²⁷

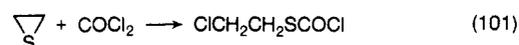


G. Reaction with Cyclic Ethers

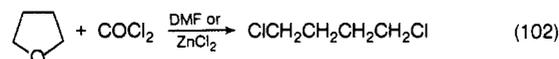
Ring opening occurs when epoxides are treated with phosgene, resulting in the formation of β -chloroethyl chloroformates.^{228,229} If an excess of epoxide is used, the corresponding carbonate is obtained.²³⁰



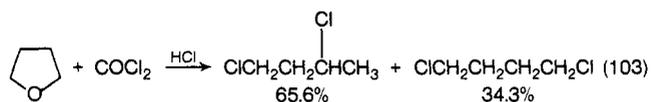
Ethylene sulfide reacts with phosgene in a similar fashion to afford β -chloroethyl chlorothioformates.²³¹



When tetrahydrofuran is treated with phosgene in the presence of *N,N*-dimethylformamide²³² or zinc chloride,²³³ ring opening occurs and 1,4-dichlorobutane is formed as the major product.



In the presence of hydrogen chloride, the major product from the reaction of phosgene with tetrahydrofuran is 1,3-dichlorobutane.²³⁴



(227) R. K. Pearson, T. W. Platt, J. C. Renforth, N. J. Sheetz, and L. J. Edwards, U. S. Atomic Energy Commission, Report No. CCC-1024-TR-277, 1957; *Chem. Abstr.*, **55**, 20791 (1961).

(228) M. S. Malinovskii and N. M. Medyantseva, *Zh. Obshch. Khim.*, **23**, 221 (1953); *Chem. Abstr.*, **48**, 2580 (1954).

(229) M. S. Malinovskii and N. M. Medyantseva, *J. Gen. Chem. USSR*, **23**, 229 (1953).

(230) J. I. Jones, *J. Chem. Soc.*, 2735 (1957).

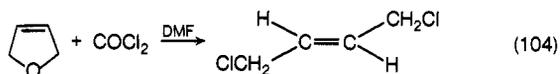
(231) G. Y. Epshtein, I. A. Vsoy, and S. Z. Iuin, *Zh. Obshch. Khim.*, **34**, 1948 (1964); *Chem. Abstr.*, **61**, 8178 (1964).

(232) W. Zeigenbein and K. Heinz, German Patent 1,188,570 (1965); *Chem. Abstr.*, **62**, 16052 (1965).

(233) V. I. Lutkova and N. I. Kutsenko, *Zh. Prikl. Khim.*, **32**, 1635 (1959); *Chem. Abstr.*, **54**, 1263 (1960).

(234) K. O. Christie and A. E. Pavlath, U. S. Patent 3,406,212 (1968); *Chem. Abstr.*, **70**, 57101 (1969).

2,5-Dihydrofuran reacts with phosgene to afford *cis*-1,4-dichloro-2-butane.²³²



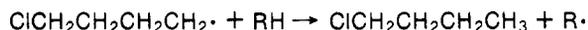
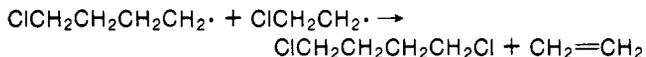
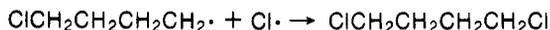
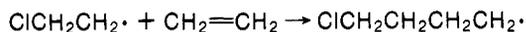
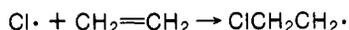
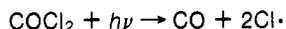
Apparently, no mechanistic studies have been done on the reactions of phosgene with tetrahydrofuran derivatives. The question of whether they are truly reactions of phosgene with the oxygen center of the cyclic ether or reactions of phosgene with products resulting from prior ring cleavage remains to be answered.

IV. Reactions at a Carbon Center

A. Homolytic Reactions of Phosgene with Hydrocarbons

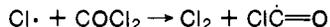
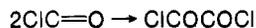
Although many papers have been published²³⁵ that describe the photodecomposition and photooxidation of phosgene, only a limited amount of work has been done on the interactions of phosgene with hydrocarbons under homolytic conditions.

The photolysis and radiolysis of phosgene in the presence of ethylene and other olefins, under a variety of conditions, have been investigated.²³⁶⁻²⁴⁴ Variables studied include mole ratios of the reactants, temperature, light intensity, and wavelength.^{237,238} The principal reactions that occur in the phosgene-ethylene system are listed below.



By extending the above reaction pattern, a variety of six carbon reaction products could be expected, and, indeed, later workers have identified them.²³⁸

It has been repeatedly stated in the literature that phosgene does not react with alkyl and chloroalkyl radicals, and that the chlorocarbonyl radical $[\text{COCl}\cdot]$ is too unstable at room temperature to result in any viable products in the presence of either olefins or alkanes. Reactions that are claimed to improbable under "photochlorination" conditions are listed below.



(235) L. Fowler and J. J. Beaver, *J. Amer. Chem. Soc.*, **75**, 4186 (1953), and references therein.

(236) M. S. Kharasch, S. S. Kane, and H. C. Brown, *J. Amer. Chem. Soc.*, **64**, 333 (1942).

(237) M. H. J. Widnen, *J. Amer. Chem. Soc.*, **83**, 3014 (1961).

(238) J. Heicklen, *J. Amer. Chem. Soc.*, **87**, 445 (1965).

(239) F. Runge, *Z. Elektrochem.*, **60**, 956 (1956); *Chem. Abstr.*, **51**, 6358 (1957).

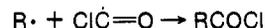
(240) M. J. Grosman, *World Petrol. Congr. Proc.*, 5th, No. 10, 85 (1960); *Chem. Abstr.*, **56**, 9606 (1962).

(241) M. Takehisa and M. Yasumoto, *Nippon Isotope Kaigi Hobun-shu*, **4**, 301 (1961); *Chem. Abstr.*, **61**, 14072 (1964).

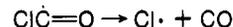
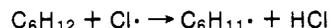
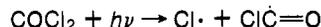
(242) S. Kambara, N. Yamazaki, A. Kaji, and T. Oikawa, *J. Chem. Soc. Jap.*, **57**, 652 (1954); *Chem. Abstr.*, **49**, 8816 (1955).

(243) H. Treibs and H. Ortmann, *Chem. Ber.*, **93**, 545 (1960).

(244) H. Treibs and H. Ortmann, *Naturwissenschaften*, **45**, 85 (1958).



An interesting exception to the above generalizations has been reported. Cyclohexane reacts with phosgene, under homolytic conditions, to form a mixture of cyclohexanecarboxyl chloride and cyclohexyl chloride.^{245,246} The products formed in this photolysis reaction are particularly dependent on the reaction temperature and the following reaction scheme has been proposed.²⁴⁶

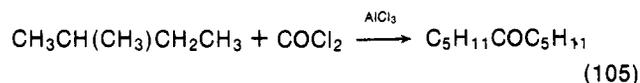


The radiolysis of 1-butene, in the presence of phosgene, is reported to proceed by a free-radical path and affords chlorobutanes, dichlorobutanes, and C_8 olefins as principal products. No C_4 or C_8 products containing the COCl group were observed, but some of the higher molecular weight products did contain this functional group.^{241,247}

B. Heterolytic Reactions of Phosgene with Hydrocarbons

1. Alkanes and Cycloalkanes

Although a number of references to the reactions of phosgene derivatives, such as carbamoyl chlorides, with alkanes have appeared,^{248,249} only one example of the use of phosgene for the acylation of alkanes has been reported.²⁵⁰ This early report describes the reaction of phosgene with various alkanes and cycloalkanes, in the presence of aluminum chloride, to afford undefined products whose elemental analyses were consistent with a dialkyl ketone structure. The ketonic structure was confirmed by reducing the products with sodium in alcohol and esterifying the resulting products with an organic acid. Although an acyl halide is an expected intermediate in this reaction, none was isolated.



2. Aromatic Hydrocarbons

The reactions of a wide variety of aromatic compounds with phosgene, in the presence of aluminum chloride, have been well documented.²⁵¹ The literature contains a number of studies aimed at making benzoic and alkylbenzoic acids by this route,²⁵²⁻²⁵⁴ but this reaction leads

(245) Soc. pour l'ind. chim. à Bale, Swiss Patent 228,931 (1943); *Chem. Abstr.*, **43**, 3033 (1949).

(246) M. S. Kharasch and H. C. Brown, *J. Amer. Chem. Soc.*, **62**, 454 (1940); **64**, 329 (1942).

(247) M. Takehisa and M. Yasumoto, *Tokyo Kogyo Shikensho Hokoku*, **61**, 190, (1966); *Chem. Abstr.*, **66**, 64803 (1967).

(248) H. Hopff, *Angew. Chem.*, **60**, 245 (1948).

(249) H. Hopff and H. Ohlinger, *Angew. Chem.*, **61**, 183 (1949).

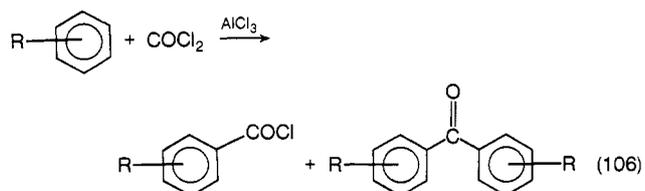
(250) A. Schaarschmidt, U. S. Patent 1,995,752 (1935); *Chem. Abstr.*, **29**, 3349 (1935).

(251) G. A. Olah, Ed., "Friedel-Crafts and Related Reactions," Vol. I-III, Wiley Interscience, New York, N. Y., 1963-1965.

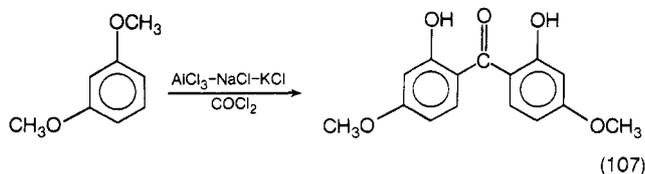
(252) R. E. Wilson and E. W. Fuller, *J. Ind. Eng. Chem.*, **14**, 406 (1922).

(253) J. F. Norris and E. W. Fuller, U. S. Patent 1,542,264 (1925).

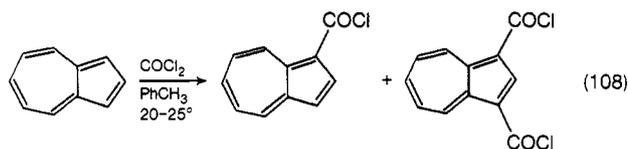
to the formation of benzophenones as the principal products²⁵⁵⁻²⁷⁰ unless a hindered substrate is used, or a special means is employed to remove the intermediate aroyl halide from the reaction mixture before it can react further.^{252-254,271} As expected, when the hydrocarbon is used as the reaction solvent, the selectivity is lowest and benzene, toluene, xylene,²⁵¹ the halobenzenes,²⁷⁰ alkoxybenzenes,^{259,260,268} and substituted anilines²⁶⁷ afford benzophenone derivatives as nearly the sole product. With electron deficient aromatics, there is an increase in the amount of aroyl halide formed.²⁶⁹ Durene and pentamethylbenzene give good yields of aroyl chlorides because of steric hindrance to further reaction.²⁷¹ Success has been reported in suppressing benzophenone formation by using a large excess of phosgene.²⁵⁴ When the reaction is carried out in carbon disulfide, fair yields of aroyl chlorides are obtained.^{252-254,271} This enhanced selectivity results from the general insolubility of the aroyl chloride-aluminum chloride complex in carbon disulfide, preventing further reaction. This approach does not work well for highly substituted benzenes, since their complexes are more soluble in the system.



An interesting reaction occurs when 1,3-dimethoxybenzene is treated with phosgene.²⁶⁸ In addition to acylation, dealkylation of a methoxy group is also observed.

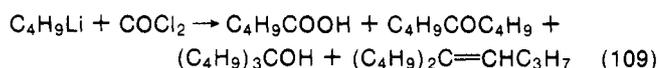


Azulene reacts with phosgene, even in the absence of a Friedel-Crafts catalyst.^{265,266} Reaction occurs at the 1 and 3 positions, at room temperature, to give good yields of azulenecarboxyl chlorides.

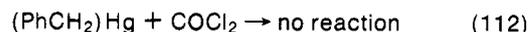
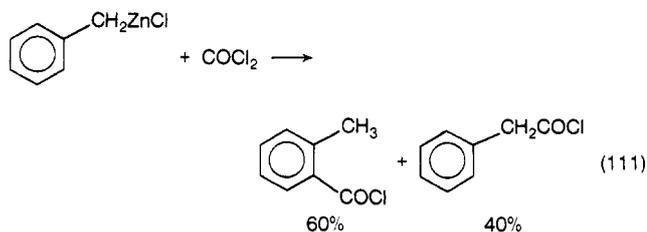
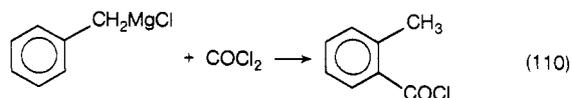


3. Organometallic Compounds

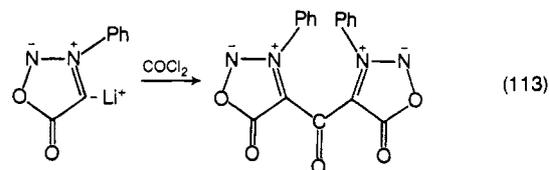
Phosgene reacts with alkylolithium^{272,273} and Grignard²⁷⁴ reagents as a typical acid chloride. Depending on the stoichiometry and the conditions, the products are, after hydrolytic work-up, carboxylic acids, symmetrical ketones, or tertiary alcohols and their dehydration products. When an aromatic organometallic is used, no dehydration occurs and the tertiary alcohol can be isolated in good yield.



An unusual rearrangement is reported to occur when benzyl Grignard reagents are treated with phosgene.²⁷⁴ The products from this reaction are primarily ring-substituted materials, and earlier work on the addition of aldehydes to benzyl Grignard reagents suggests that this rearrangement takes place during the addition of phosgene to the organometallic.^{275,276} Benzylzinc chloride reacts with phosgene to give a mixture of normal and rearranged product, while dibenzylmercury does not react.



Lithium phenylsydnone reacts with phosgene in the conventional manner to give good yields of the corresponding ketone.²⁷⁷



An interesting acylation reaction occurs when 2,6-di-tert-butyl-4-methylphenol is treated with phosgene in the presence of potassium hydroxide.²⁷⁸ Instead of yielding

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(260) F. Mauthner, *J. Prakt. Chem.*, **87**, 403 (1913).

(261) E. Ador and F. Meier, *Chem. Ber.*, **12**, 1968 (1879).

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(266) W. Triebs, H. J. Neupert, and J. Hiebsch, *Chem. Ber.*, **92**, 1216 (1959).

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(270) Y. Hayashi, *J. Soc. Chem. Ind. Jap.*, **47**, 536 (1944); *Chem. Abstr.*, **42**, 6772 (1948).

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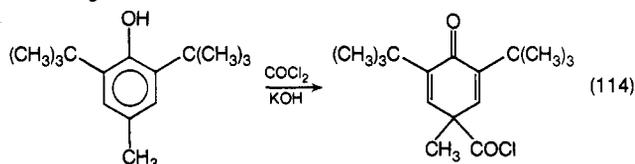
(275) W. G. Young and S. Siegel, *J. Amer. Chem. Soc.*, **66**, 354 (1944).

(276) S. Siegel, W. M. Boyer, and R. R. Jay, *J. Amer. Chem. Soc.*, **73**, 3237 (1951).

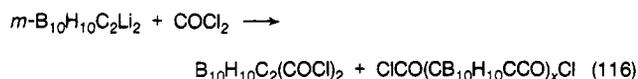
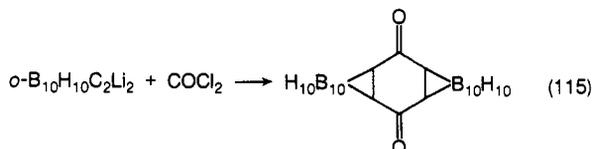
(277) N. Suci, G. Mihal, M. Eljan, and E. Stroescu, *Tetrahedron*, **21**, 1369 (1965).

(278) H. A. Stansbury, Jr., and R. F. Cantrell, *J. Org. Chem.*, **32**, 824 (1967).

the expected chloroformate, acylation occurs at the 4 position to give an acid chloride.



Lithium carboranes react with phosgene to give simple carbonyl derivatives of the carborane.²⁷⁹ Depending on the nature of the starting material, both acid chlorides and ketones can be formed.

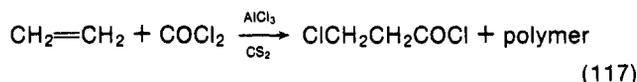


C. Addition to Multiple Bonds

1. Carbon-Carbon Multiple Bonds

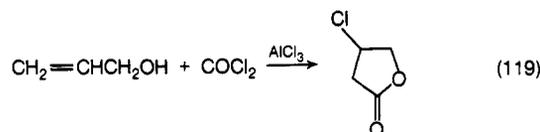
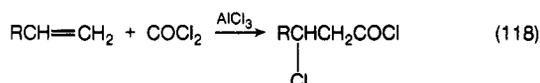
The reactions of olefins with acyl halides have recently been reviewed,²⁸⁰ but the analogous reactions of phosgene have received little attention.

Early workers²⁸¹ reported that phosgene reacts with ethylene, in the presence of aluminum chloride, to afford β -chloropropionyl chloride in good yield. Toluene was used as a solvent in this reaction, and later workers²⁸²⁻²⁸⁶ could only isolate products resulting from the reaction of phosgene and ethylene with the solvent, with none of the desired acid chloride being observed. However, by using carbon disulfide as a solvent, low yields of β -chloropropionyl chloride could be prepared.²⁸⁴⁻²⁸⁶ Attempts to carry out the reaction in carbon tetrachloride or chlorobenzene, and to use zinc chloride as a catalyst, were unsuccessful. Interestingly, the higher the ethylene concentration used in this reaction, the lower the yield of acid chloride, a result of increased ethylene polymerization.

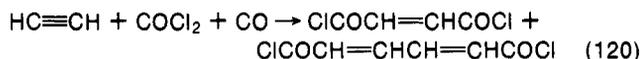


In addition to the reaction of phosgene with ethylene, excellent yields of β -chloro acid chlorides have been reported to be formed from propylene,²⁸⁷ styrene,²³⁵ and 2-methyl-1-butene.²³⁵ The formation of β -chloro lactones from the reaction of allyl alcohol derivatives with phosgene has also been reported.²³⁵ In light of the work on the reactions of ethylene, these results must be viewed

with some skepticism. To our knowledge, no attempts have been made to verify these results.

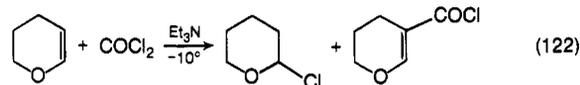
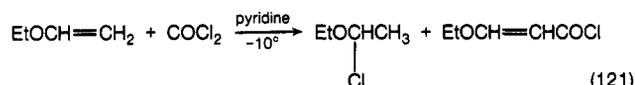


The palladium-catalyzed reaction of phosgene with acetylene, in the presence of carbon monoxide, and under pressure, has been reported to give good yields of fumaric and muconic acid chlorides.²⁸⁸



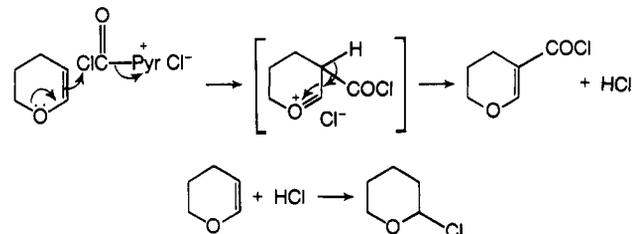
The uncatalyzed reaction of phosgene with acetylene, in the absence of carbon monoxide and oxygen, leads to the formation of a complex product of undefined structure which can be used in molding compounds.²⁸⁹

Phosgene reacts with acyclic and heterocyclic vinyl ethers, in the presence of catalytic amounts of tertiary amines, to give a mixture of β -alkoxyacrylic acid derivatives and α -chloro ethers.^{290,291}



Although no mechanistic studies have been done, this reaction might be explained by Scheme IV.

SCHEME IV



The addition of phosgene to enamines has recently been reported,²⁹²⁻²⁹⁵ and the example given in Scheme V is illustrative of this general reaction. The iminium salt that is initially formed is readily converted to the chloroformyl enamine in the presence of base. The final products were isolated as their methyl esters and were identical with those obtained by the acylation of the enamine with methyl chloroformate.

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(281) E. Pace, *Gazz. Chim. Ital.*, **59**, 578 (1929); *Chem. Abstr.*, **24**, 338 (1930).

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(283) S. L. Varschavski and E. A. Doroganyevskaya, *Gazz. Chim. Ital.*, **64**, 53 (1934); *Chem. Abstr.*, **28**, 5043 (1934).

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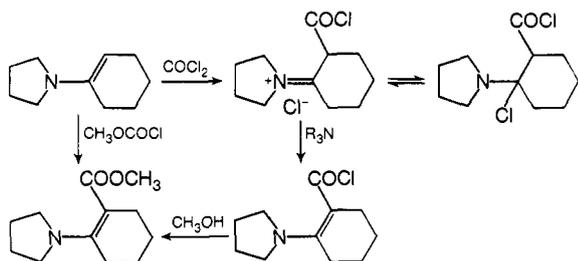
(292) R. Buyle and H. G. Viehe, *Tetrahedron*, **24**, 3987 and 4217 (1968).

(293) A. Halleux and H. G. Viehe, *J. Chem. Soc. C*, 881 (1970).

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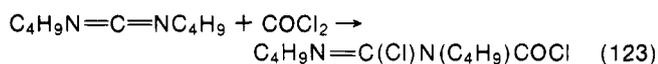
(295) N. N. Sveshnikov and N. A. Damir, *Dokl. Akad. Nauk SSSR*, **164**, 1077 (1965); *Chem. Abstr.*, **64**, 3470 (1966).

SCHEME V



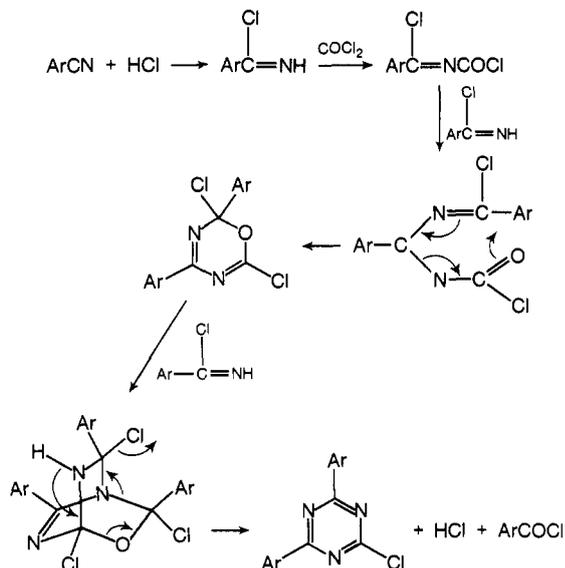
2. Carbon-Nitrogen Multiple Bonds

The addition of phosgene to the multiple bond system of carbodimides has recently been reported^{296,297} and is illustrated in eq 123. The resultant chloroformamidine derivatives are stable materials that can even be purified by vacuum distillation.



In the presence of hydrogen chloride, phosgene reacts with aryl nitriles to give good yields of 2-chloro-4,6-diaryl-1,3,5-triazines and benzoyl chloride.²⁹⁸ When benzonitrile was used as a starting material, analysis of the reaction mixture showed the presence of *N*-(1-chlorobenzylidene)carbamoyl chloride. This intermediate was isolated, and when allowed to react with benzonitrile, in the presence of hydrogen chloride, gave the expected triazine. This evidence, in addition to some ¹⁴C tracer experiments, led to the mechanism of Scheme VI for the reaction.

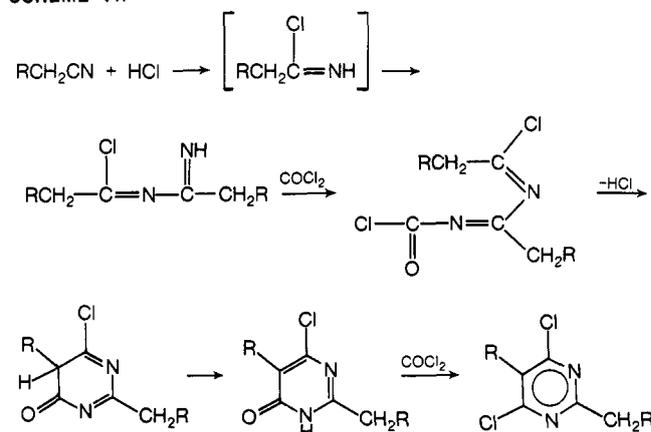
SCHEME VI



Aliphatic nitriles, having at least one α -hydrogen atom, react with phosgene, in the presence of hydrogen chloride, to produce good yields of 6-chloro-2,5-dialkyl-4(3*H*)-pyrimidine hydrochlorides.^{299,300} Small amounts of the

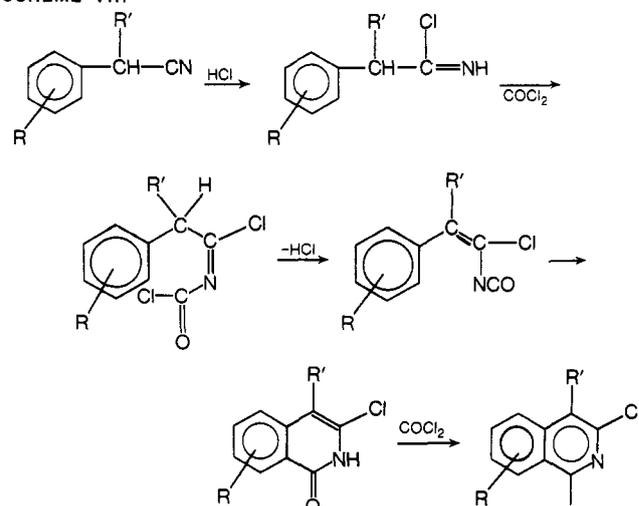
4,6-dichloro derivatives are generated by further reaction of the initial product with phosgene. Scheme VII has been proposed.

SCHEME VII

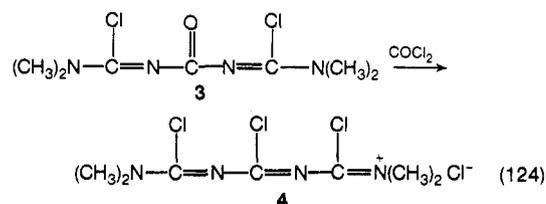
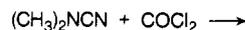


When an arylacetoneitrile is treated with phosgene, in the presence of excess hydrogen chloride, the principal product is a 1,3-dichloroisoquinoline, formed by cyclization of an intermediate carbamoyl chloride as shown in Scheme VIII.³⁰¹

SCHEME VIII



Phosgene is reported³⁰² to react with dimethylcyanamide to give good yields of the complex chloroformidinium chloride (4). Compound 3 is believed to be an intermediate in this reaction.



V. Reactions of Phosgene with Inorganic Compounds

The usual method for removing phosgene from process waste gases is by water hydrolysis. Concentrated sodium

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Phosgene has been reported to form stable, well-defined, 1:1 complexes with Lewis acids such as aluminum chloride,³⁴⁴⁻³⁴⁹ boron halides,^{349,350} thionyl chloride,³⁵¹ antimony chloride,^{346,349} and tin chlorides.³⁴⁹ The complex with aluminum chloride has been studied most extensively, and these studies demonstrate that phosgene is coordinated to the metal in such a way that the chlorine atoms of phosgene do not lose their integrity.^{344,347}

The literature also makes reference to the recovery of platinum metal from spent catalysts by treatment with phosgene to form a volatile "carbonyl chloride complex," followed by hydrolytic hydrogenation to reprecipitate the platinum.³⁵²

VI. Disproportionation of Phosgene

When phosgene is heated in the presence of activated carbon,³⁵³ or a variety of metal catalysts,³⁵³⁻³⁵⁸ disproportionation occurs to yield carbon tetrachloride as the major product.



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VII. Summary

Quite apart from the wide-spread commercial use of phosgene as an acylating agent (isocyanate and chloroformate chemistry), the literature abounds with references on the interaction of phosgene with a broad spectrum of organic functional groups. In our review we have examined these reactions and categorized according to the point of attack by phosgene. Thus, phosgene reacts with a multitude of nitrogen, oxygen, sulfur and carbon centers, as well as with a variety of inorganic compounds. The diversity of reactions that phosgene undergoes includes acylation, chlorination, decarboxylation, and dehydration reactions, all of which have been discussed. While compiling this review, we came to the conclusion that more in-depth studies of phosgene chemistry should be made. We believe that the potential of phosgene as a useful (and interesting) chemical intermediate has not been realized. It is our hope that this paper will serve to stimulate more research on the chemistry of phosgene.

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